



Published in final edited form as:

J Pediatr. 2016 July ; 174: 282. doi:10.1016/j.jpeds.2016.04.086.

Diagnosis of adrenal insufficiency in eosinophilic esophagitis: The importance of timing of cortisol measurements in interpreting low-dose adrenocorticotrophic hormone stimulation testing

Melissa J. Schoelwer, MD and Todd D. Nebesio, MD

Indiana University School of Medicine, Riley Hospital for Children, Indianapolis, Indiana

To the Editor

Golekoh et al¹ reported adrenal insufficiency (AI) in 10% of children with eosinophilic esophagitis treated with swallowed glucocorticoids for 6 months and suggest screening this population with low-dose adrenocorticotrophic hormone stimulation testing (LDST).

Although this report provides important information on an at-risk population, we have concerns with the way the LDST was performed and thus question the rate of AI reported. Cortisol was measured only once after administration of synthetic adrenocorticotrophic hormone at 20 minutes.

Peak cortisol tends to be earlier with LDST (1 µg) compared with high-dose (250 µg) stimulation testing, with the greatest mean cortisol concentrations occurring at 30 minutes.^{2,3} Additional studies have shown that the peak cortisol concentration during LDST may occur at 30 minutes, 35 minutes, 40 minutes, or even up to 60 minutes.^{4–6} Cartaya and Misra⁶ retrospectively examined the results of LDST in 82 pediatric patients and found that 54% attained a peak cortisol at 60 minutes. Importantly, 11 patients who did not pass at 30 minutes did so at 60 minutes. In addition, children who were normal weight or underweight tended to peak at 60 minutes ($P = .01$), and in the study by Golekoh et al,¹ patients with abnormal responses to LDST had significantly lower body mass index z scores compared with those with a normal response. Therefore, because cortisol values were not measured at later time points, children in the study by Golekoh et al¹ may have been misclassified as having AI.

The timing of cortisol sampling is important to correctly interpret a LDST. Assessment with just a 20-minute cortisol value can result in over diagnosis of AI and an increased number of false positives, leading to unnecessary treatment with maintenance or stress glucocorticoids and potentially lead to unwanted side effects.

References

1. Golekoh MC, Hornung LN, Mikkala VA, Khoury JC, Putnam PE, Backeljauw PF. Adrenal insufficiency after chronic swallowed glucocorticoid therapy for eosinophilic esophagitis. *J Pediatr*. 2016; 170:240–5. [PubMed: 26687577]

2. Dickstein G, Shechner C, Nicholson WE, Rosner I, Shen-Orr Z, Adawi F, et al. Adrenocorticotropin stimulation test: effects of basal cortisol level, time of day, and suggested new sensitive low dose test. *J Clin Endocrinol Metab.* 1991; 72:773–8. [PubMed: 2005201]
3. Weintrob N, Sprecher E, Josefsberg Z, Weininger C, Aurbach-Klipper Y, Lazard D, et al. Standard and low-dose short adrenocorticotropin test compared with insulin-induced hypoglycemia for assessment of the hypothalamic-pituitary-adrenal axis in children with idiopathic multiple pituitary hormone deficiencies. *J Clin Endocrinol Metab.* 1998; 83:88–92. [PubMed: 9435421]
4. Rasmuson S, Olsson T, Hagg E. A low dose ACTH test to assess the function of the hypothalamic-pituitary-adrenal axis. *Clin Endocrinol (Oxf).* 1996; 44:151–6. [PubMed: 8849568]
5. Park YJ, Park KS, Kim JH, Shin CS, Kim SY, Lee HK. Reproducibility of the cortisol response to stimulation with the low dose (1 microg) of ACTH. *Clin Endocrinol (Oxf).* 1999; 51:153–8. [PubMed: 10468984]
6. Cartaya J, Misra M. The low-dose acth stimulation test: is 30 minutes long enough? *Endocr Pract.* 2015; 21:508–13. [PubMed: 25667371]